SHOCK AND HEMORRHAGE*

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The following description of the clinical picture of shock was given by Samuel D. Gross in 1872. "The person, although severely injured, congratulates himself upon having made an excellent escape, and imagines that he is not only in no danger, but that he will soon be about again; in fact, to look at him, one would hardly suppose, at first sight, that there was anything serious the matter; the countenance appears well, the breathing is good, the pulse is but little affected, except that it is too soft and frequent, and the mind, calm and collected, possesses its wonted vigor, the patient asking and answering questions very much as in health. But a more careful examination soon serves to show that deep mischief is lurking in the system; that the machinery of life has been rudely unhinged, and that the whole system is profoundly shocked; in a word that the nervous fluid has been exhausted and that there is not enough power in the constitution to reproduce and maintain it. The skin of such a person assumes an icterode, or sallow, cadaverous appearance, feeling at the same time doughy and inelastic; the extremities are deadly cold; the pulse makes a desperate effort at reaction, but is, at best, weak and tranquil for one who has sustained such an amount of violence. The system does not seem to be conscious of what has occurred; its sensibilities are blunted, and it is incapable of suffering. Nature, to use the language of Hunter, does not feel the injury." There have been advances in our knowledge concerning the mechanism of the production of shock since 1870, but this description of the clinical picture by Gross could not be improved upon at the present time.

Since the World War shock has been divided grossly into two types. Primary shock refers to the condition in which a decline in blood pressure is noted immediately following the receipt of an injury. A satisfactory explanation for this condition seems to have been offered by Goltz in

* Delivered October 19, 1936.

experiments in which it was found that the essential alteration was a vasodilatation. Secondary shock refers to the type in which the interval separating the injury and the decline in blood pressure is usually an hour or longer. It has been in an effort to explain this condition that most of the theories have been advanced. Perhaps the most divergent views have been expressed by those who maintain that shock is associated with a general relaxation of the vessels and by those who state that it is accompanied by vasoconstriction. Evidence of a convincing nature has been offered to show that secondary shock except in the terminal stages is associated with vasoconstriction. The proven facts in the case are that it is accompanied by a diminution in the blood volume and a decrease in the blood pressure. As a result of these findings, most of the theories have become untenable. During the past fifteen years, the toxemia theory has been rather generally accepted. This theory differs from the others which consider a diminution in the blood volume, vasoconstriction and capillary congestion as the essential disturbances in secondary shock in that evidence as to the initiating agent is suggested. It has in common with other theories the fact that no initiating agent has actually been demonstrated.

The most often quoted experiments that had to do with the formulating of the toxemia theory are those that were performed by Cannon and Bayliss in which shock was produced by traumatizing one of the posterior extremities of anesthetized cats. Following the death of the animals the injured and non-injured extremities were amputated by symmetrical cuts across the upper thighs, they were weighed and the difference in weight was determined. They found that there was not a sufficient difference in weight to account for the decline in blood pressure and death by the loss of blood into the injured area. Section of the spinal cord in the upper lumbar region, in some experiments, showed that the fall in blood pressure was not due to any general effect of the trauma on the circulation, brought about by nervous agencies. The decline in blood pressure

could not be explained on the basis of fat embolism, acapnia or acidosis. It was assumed that the continued fall in blood pressure was due to the absorption of some depressant substance from the injured area into the general circulation. The effects of injecting histamine and of traumatizing muscles were compared in various experiments and it was believed that the hypothetical depressant produced by injuring muscles was either histamine or some closely related substance.

I repeated the experiments of Cannon and Bayliss using deeply anesthetized dogs instead of cats. It was observed that the swelling which followed the injury was not limited to the area directly traumatized but extended into the loose tissues of the groin and flank. Hence it seemed that their amputations had not been performed at a sufficiently high level if the entire loss of blood and lymph into the injured part were to be determined. The method which I used was briefly as follows: A midline abdominal incision was made. The symphysis pubis was divided in the midline. The bladder and rectum were removed. The aorta and inferior vena cava were doubly ligated and divided. A posterior midline incision was made and the lower portion of the body was divided into two parts, the tail being discarded.

The difference in the weights of the traumatized and non-traumatized extremities in these experiments showed that approximately one half of the total blood volume had been lost into the injured part, which was sufficient by itself to account for the decline in pressure. Similar results were obtained by Parsons and Phemister.

Many other experiments of a somewhat different nature were performed. One of these consisted of isolating the femoral artery in the groin, placing a tourniquet around the upper thigh constricting all structures save the artery and of traumatizing the thigh distal to the tourniquet. In these experiments there was no possibility for the absorption of toxic products from the injured part. Death occurred several hours following the traumatization and it was found that there was a loss of a sufficient part of the blood volume into the injured part to have caused it.

In other experiments, the effects of milder trauma to an extremity, of trauma to the intestines and of burns were studied. Analysis of the fluid that escaped into or from the injured area in these experiments was carried out by Dr. Beard and others. It is to be noted in the experiments in which the intestines were traumatized that the fluid escaping into the peritoneal cavity had approximately the same composition in protein as the blood plasma. This was true of other constituents as well. The protein content is emphasized because it is protein which attracts fluid to the blood stream and holds it there, which is all important in maintaining the blood volume.

I shall consider in detail only the experiments in which burns were produced. These studies were performed on animals profoundly anesthetized with sodium barbital. The animals did not blister when burned but the skin became leather-like and fluid accumulated in the subcutaneous tissues. As has been stated, this fluid is blood plasma. The amount of this fluid was determined as follows: Only one half of the body surface was burned. Following the death of the animals, which in our experiments occurred after an average interval of fifteen hours, the body was divided into two parts by anterior and posterior incisions. The internal organs and head were discarded, and the difference in the weights of the two parts was determined. The average difference in weight equalled 3.34 per cent of the total body weight, the burned side always being the heavier. A comparison with the results of other experiments in which death was produced by the removal of blood plasma, shows that the collection of blood plasma at the site of the burn was sufficient to account for the decline in blood volume and death. It is my belief that fatalities in the human which occur within thirty-six hours following burns are due to the loss in blood plasma and the accompanying increase in the concentration of the red blood cells. Deaths which occur a number of days later are probably due to other factors.

In association with Dr. Johnson the effects on the cardiac output and blood pressure of hemorrhage, of muscle trauma, and of histamine administration were studied. Taking up first the effects of hemorrhage, it was observed that following the removal of blood equalling 27 cc. per kilogram of body weight the output of the heart had diminished considerably whereas there was very little alteration in the blood pressure. Forty minutes following the traumatization of an extremity, it was noted that the output of the heart had declined greatly whereas there was very little alteration in the blood pressure. On the other hand following the administration of histamine the blood pressure declined first and the output of the heart subsequently. Burch and Harrison found that the injection of large amounts of novocain into the spinal canal produces alterations similar to those that are produced by the injection of histamine. I have recently found that primary shock and bilateral adrenalectomy also are accompanied by similar alterations. Trauma to the central nervous system is usually accompanied by a simultaneous decline in the cardiac output and blood pressure. The only point which I wish to emphasize here is that uncomplicated hemorrhage and trauma to an extremity are both associated with first, a decrease in the output of the heart followed later by a decline in the blood pressure, while the alterations appear in the reverse order as a result of the injection of histamine.

Results of a somewhat similar nature were found by Roome, Keith and Phemister in experiments in which a low blood pressure was produced by a variety of procedures which included, hemorrhage, trauma to an extremity, plasmaphaeresis, histamine administration, etc. After the pressure had been reduced to a low level, the quantity of blood that it was necessary to remove in order to cause death was determined. Following hemorrhage and trauma, it was found that the removal of a relatively small volume of blood resulted in death whereas it was necessary to remove larger quantities when the pressure had been caused to decline by histamine administration.

If the observations which I cited are correct, then one may ask why it is that the criteria of shock and hemorrhage are not identical. As an example of the belief that they are not identical, it is usually stated that shock is associated with an increase in the concentration of the red blood cells, with no response to the transfusion of blood and with capillary congestion and hemorrhage in the tissues. On the other hand, hemorrhage is said to be associated with a dilution of the red blood cells, with a favorable response to transfusion and with an anemic appearance of the tissues. Evidence will be presented which shows that some of these statements are erroneous.

Experiments were performed on dogs in which the blood pressure was gradually reduced to a low level by the slow withdrawal of blood from the femoral artery. No anesthesia was used in these experiments except for the injection of novocain at the sites where the cannulae were introduced. After having produced a sustained decline in the pressure to approximately 70 mm. of mercury, the animal was allowed to die without having further blood removed. The desired condition was to have the blood pressure remain at a low level as long as possible preceding death. Usually death occurred approximately an hour after a sustained reduction in the pressure had been obtained. Capillary congestion and hemorrhage were noted in some of the organs at autopsy. An increase in the concentration of the red blood cells occurred in a few experiments.

A low blood pressure of longer duration was produced in other experiments. The pressure was reduced by the removal of blood from the femoral artery and death was delayed by the introduction of blood by the direct method from a suitable donor. If the blood pressure rose above 70 mm. of mercury further blood was removed. If death seemed imminent, a small quantity of blood was withdrawn from the donor and injected intravenously. In this manner, the blood pressure was maintained at a low level for several hours before death occurred. No evidence that the blood was incompatible was observed. The blood pressure records in these experiments were quite similar to those

that were obtained when an extremity was traumatized. All of the animals died despite the fact that more blood was introduced than was removed. In other words, after the blood pressure remained at a low point for several hours, transfusion was without benefit. An increase in the concentration of the red blood cells was found in all experiments. Capillary congestion and hemorrhage and necrosis were present in many of the tissues of the body. Particularly striking was the presence of free blood in the lumen of the intestinal tract.

Thus it is to be noted that an increase in the concentration of the blood, a negative response to transfusion, and marked alterations in the tissues in the body can be produced by hemorrhage and that they are not peculiar to traumatic shock.

In the care of patients, one rarely encounters as a result of hemorrhage a low blood pressure that persists for several hours. If bleeding from a large blood vessel takes place, usually either early death occurs or the loss of blood is stopped and recovery follows. If the bleeding results in almost immediate death, an anemic appearance of the tissues is found at autopsy. If the bleeding is controlled, usually the remaining volume of blood is augmented by the passage of fluids from the tissue spaces into the blood stream or fluid is added artificially, and a rise in the blood pressure and a decrease in the concentration of the blood occur. A somewhat different set of conditions is encountered when fluid is lost from many small vessels into an injured part. The speed with which fluid leaves the blood vessels is usually slower because of the small size of the vessels and because of the pressure in the tissue spaces. As the pressure in the blood vessels diminishes and the pressure in the tissue spaces increases, the loss of fluid locally is still further retarded. The fluid that is lost has a larger proportion of plasma and a smaller proportion of red blood cells than that existing in the blood stream. This accounts partially for the increase in the concentration of the blood. Since the blood pressure usually remains at a low point for a considerable time preceding death

following trauma to large masses of muscle, the tissues of the body are partially deprived of blood and oxygen and alterations such as capillary congestion and dilatation and hemorrhage take place.

These observations explain why the treatment of severe shock is so unsatisfactory. After damage has resulted from an inadequate supply of blood to the tissues for a considerable time, regardless of the cause, fluids introduced into the blood stream will escape. As apparent exceptions to this statement, one observes occasionally the recovery of patients in whom the blood pressure has remained at a low level for a long time.

There may be various contributory factors which are partially responsible for the production and maintenance of shock. Food and water deprivation and exposure to cold increase the ease with which it can be produced. Prolonged anesthesia may greatly exaggerate the condition. I have observed recently that profound anesthetization with ether for six hours results in capillary hemorrhage and congestion in many of the organs of the experimental animal. Just as a serious illness reduces one's ability to withstand the loss of blood, similarly it lessens the amount of trauma that can be tolerated.

I would like to make several additional remarks concerning the treatment of shock. Drugs which constrict arterioles raise the blood pressure but do not increase the blood volume and that is what one wishes to accomplish. Vasoconstrictor drugs are of little value except in shock accompanied by vasodilatation. If one is to increase the blood volume, fluids must be introduced.

As regards the choice of fluid, the following study is of interest. In this experiment, a large quantity of salt solution was introduced intravenously while the intestines were being traumatized. It is to be noted that not only did most of the salt solution escape but that it carried a great deal of protein with it, thus diminishing the protein content of the blood plasma and decreasing the osmotic pressure. Blood is much the better fluid to inject for even though a large part of it escapes through the injured

capillaries, that remaining in the blood stream maintains a normal protein content as protein is present in the blood that is introduced. Andrus and Heuer have obtained encouraging results with the use of extracts of the adrenal cortex.

We have attempted a classification of acute circulatory failure from a physiological viewpoint. The modern tendency in surgery is to classify all forms of acute circulatory failure complicating operations and wounds, except organic heart failure, under the head of shock. The terms that have been used to designate the different types are:

Hematogenic Type. First to be considered is the hematogenic type. The initial and the most important circulatory change is the diminution in the blood volume. It is with the hematogenic type of shock that this paper is largely concerned. Shock as a result of uncomplicated hemorrhage is the simplest example. Shock following trauma to large masses of muscle belongs to this group, if my experiments and those of Parsons and Phemister have been interpreted correctly.

Neurogenic Type. This term is used to designate the condition that is usually known as primary shock or collapse. It is more rapid in onset than the hematogenic type. The primary alteration is vasodilatation dependent on diminished constrictor tone as a result of influences acting through the nervous system.

Vasogenic Type. Vascular dilatation may be brought about by agencies which act directly on the vessels. Histamine probably exerts the major portion of its effect in this manner.

Cardiogenic Type. Acute circulatory failure as a result of primary disturbance of the heart occurs rarely. It is characterized by venous distention in contrast to the collapsed condition of veins that is found in peripheral circulatory failure. A rapid accumulation of fluid in the pericardial cavity produces this type of alteration.

A number of workers have repeated our experiments on severe trauma using similar anesthetics and have obtained similar findings. However, O'Shaugnessy and Slome using lighter anesthesia claim that it is necessary to invoke a nervous factor. They think that the loss of fluid at the site of injury is the most important factor but that it is necessary to add the neurogenic forces. Although another group in England has failed to confirm their results, I believe they contain important findings and cannot be dismissed lightly.

Freeman of this country considers vasoconstriction as probably the most important of the initiating factors in the production of shock. Even if it is an auxiliary subsequently, vasoconstriction delays the decline in blood pressure and the development of shock following hemorrhage by diminishing the calibre of the blood vessels. Swingle and his associates have reported that deficiency of adrenal cortex hormone results in increased permeability of capillaries and loss of plasma with blood concentration and serious reduction in circulating blood volume. They assume that this plays a role in surgical shock but proof of this view is lacking.

I would like to make several additional remarks concerning the first type, namely hematogenic shock. The initial and the most important circulatory change is the diminution in the blood volume. Unless the initial decrease in blood volume is too great, compensatory vasoconstriction maintains the arterial blood pressure at or near the normal level. The decline in blood volume is followed by a decrease in the return of blood to the heart and hence in a decrease in the cardiac output. If the volume of circulating blood continues to diminish, the blood pressure declines even though vasoconstriction is maintained. If the blood pressure remains depressed for a considerable time, the vasoconstrictor mechanism fails and vasodilatation results. When this stage has been reached, many other factors enter into the picture and make the condition worse. Most of these factors are probably common to all types of severe

shock regardless of the mechanism of the production. These include an insufficent supply of oxygen to the tissues with resulting damage, a decrease in the production of heat, an increase in the viscosity of the blood, an increase in capillary permeability, a diminution in the alkali reserve and probably the accumulation of toxic products. I think we can say with safety that histamine is not the cause in most instances. Muscle has a very low content of depressor substances. The amount of these substances necessary to produce shock could be obtained only by careful extraction from a mass of muscle greater than the entire weight of the animal (Slome). Recently, Sir Henry Dale made the following statement, "With regard to a possible role of histamine, we know now, what we did not know then, that of all the major tissues of the body, the muscles contain least of that substance. Whatever else it may have been, the shock following the Bayliss-Cannon limb trauma was not histamine poisoning."

As regards the second type, neurogenic shock, it is seen typically in the fainting which accompanies emotional distress or minor injuries. A similiar collapse may occur when the upper abdomen is opened and explored or in association with operations on the brain. The shock is explained by sudden inhibition of vasoconstrictor tone of central origin. The blood pressure may remain at a low level for an hour or more and then may rise spontaneously or following the giving of a vasoconstrictor drug with no subsequent ill effect. A similar fall of pressure in hematogenic shock would be a matter of grave concern. Neurogenic shock is associated with a reduction in blood pressure, with little or no decline in the blood volume and an adequate flow of blood to the vital centers is maintained for a much longer time than in the hematogenic type.

There are many instances of shock which are not so simple and which cannot be placed in any single one of these four types but are rather combinations of several of them. An example of this is the shock which follows the perforation of peptic ulcers. We have simulated this con-

dition experimentally by collecting and introducing into the peritoneal cavities of other dogs the various juices which empty into the stomach and duodenum. All of the animals became quite ill immediately following the introduction of one or more of the upper intestinal juices. The condition then seemed to improve for a while and became worse later as is frequently observed in the human following the perforation of a peptic ulcer. The most severe reactions were observed following the introduction of bile or pancreatic juice and the combination of the two exerted more ill effects than an equal volume of either of them alone. It seems possible that the pancreatic juice is actuated by the bile, thus increasing the total of the effects. The changes in the cardiac output and blood pressure produced by the introduction of the juices were studied. Although the results were not identical in all instances, it can be stated that the major primary alteration was a decline in the blood pressure, as is found in primary shock, and the subsequent change consisted of a greater drop in the cardiac output than in the blood pressure, as is found in secondary shock.

The initial signs and symptoms that were observed following the intraperitoneal injections appear too early to be explained by the absorption of toxic material. It seems likely that the most important of the early actions of the juices is that of a chemical irritant. This results in a dilatation of many small intraperitoneal vessels and I believe that it is brought about mainly by direct action on the vessels rather than through nerves, although both methods are probably concerned. At any rate, an early decline in the blood pressure is usually observed. After the blood volume decreases as a result of the marked increase in the circulatory bed and the passage of fluid into the peritoneal cavity, the output of the heart diminishes. The blood pressure is probably prevented temporarily from declining further by vasoconstriction elsewhere.

I wish to emphasize again the fact that the mechanism of the production of all instances of shock is not the same, and they cannot all be satisfactorily explained by one

theory. Dr. Ewing recently said, "There is no one cause of cancer", and I think the same statement may be made with safety in regard to shock. That which develops following trauma to an extremity is a simple example in that the decline in blood volume is due certainly in the main to the loss of blood and plasma at the site of injury. It has been shown that the condition which develops following the perforation of peptic ulcers is not as simple to explain. Many different agencies may enter into the production of shock that is associated with operations. Among these may be included, hemorrhage, sweating, the anesthetic, loss of plasma from exposed surfaces, the pooling of blood in vessels that are dilated as a result of mechanical irritation or nervous reflexes, infection and the diseases for which the operation is performed.

In conclusion, the term shock should be used to designate a clinical syndrome that is familiar to all. The pallor, apathy, sweating, cold skin, vomiting and weak pulse form part of the fully developed picture. The work of recent years has shown that it is dependent on an inadequate supply of blood to the tissues, which may be brought about by the most diverse causes.

DEATHS OF FELLOWS OF THE ACADEMY

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Dr. Robinson was gynecologist to the Beth Israel Hospital and chief gynecologist and obstetrician to the Beth Moses Hospital. He was a Fellow of the American College of Surgeons, the American Medical Association and held a certificate of the American Board of Obstetrics and Gynecology. He was also a member of the County and State Medical Societies.

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